Calming Saturn's Storms

Using Low-Dose Ketamine to Boost Neuroplasticity and Improve DBT-PTSD Treatment Outcomes for People with Borderline Personality Disorder

A research proposal

Abstract

In 2020, Dr. Martin Bohus, professor of psychosomatic and psychotherapy at Heidelberg University, Germany; expert in complex traumatic conditions; and colleague to Marsha Linehan, creator of DBT, conducted an efficacious trial at Harvard's McLean Hospital, leading to an evidence-based treatment for the non-clinical entity of complex post-traumatic stress disorder (C-PTSD). This trial, intended for sufferers of C-PTSD, also included a small cohort of participants diagnosed with BPD who responded positively.
A diagnosis of BPD was once considered the kiss of death; it is a condition that psychotherapists have continuously struggled to understand, to treat, and, indeed, even avoid. Yet, with the advent of DBT, sufferers of BPD have a path toward recovery, albeit long and arduous, as its creator, Marsha Linehan, states recovery may take 8–16 years of twice-a-week sessions.
Psychedelic science, now deservedly moving into the mainstream, has found little efficacy in the treatment of personality disorders through psychedelic-assisted therapy (PAT). One trait the DSM-5 mentions regarding BPD is the presentation of an unstable self. This instability regarding a sense of identity and self-concept inhibits psychedelic experience efficacy; however, drug efficacy in the form of increased neuroplastic potential remains. One substance under the psychedelic umbrella with a proven track record of boosting neuroplasticity is ketamine.
DBT-PTSD is an accelerated 35-session modality combining prolonged exposure therapy (PE), elements of DBT, and compassion-based psychotherapy addressing betrayal trauma. While not designed specifically for patients with BPD, evidence suggests limited efficacy in this population, which may be increased, perhaps dramatically, with the introduction of a neuroplasticity-enhancing agent capable of rapidly creating new neural pathways during therapy, potentially reducing recovery time from 8–16 years to 45 days.

BPD Diagnostic Criteria

Borderline Personality Disorder is a Cluster B personality disorder in the Diagnostic and Statistical Manual. Within this cluster, we also see antisocial, histrionic, and narcissistic personality disorders. This cluster is called the erratic cluster; other common names include the dramatic or emotional cluster.
With this disorder, we see nine symptom criteria:

- **Frantic efforts to avoid abandonment (real or imagined)**
- **Unstable relationship patterns**
- **Identity disturbance**
- **Impulsivity in at least two areas that can be self-damaging (substance abuse, reckless driving, etc.)**
- **Suicidal behavior, threats, ideations, gestures**
- **Affective instability**
- **A chronic feeling of emptiness**
- **Intense and inappropriate anger**
- **Paranoid ideation or dissociation**

In addition, BPD tends to be comorbid with substance use disorder (SUD), as well as with other Cluster B disorders, PTSD, and depression.
The severity of BPD can vary; certain symptoms may not be present in all manifestations, as only five criteria are needed for a diagnosis. This method of diagnosis is not without flaws, as it has exposed a polythetic problem and a potential need to reconvene on the matter of reconsidering orders of importance

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Low-Dose Ketamine Infusion Therapy

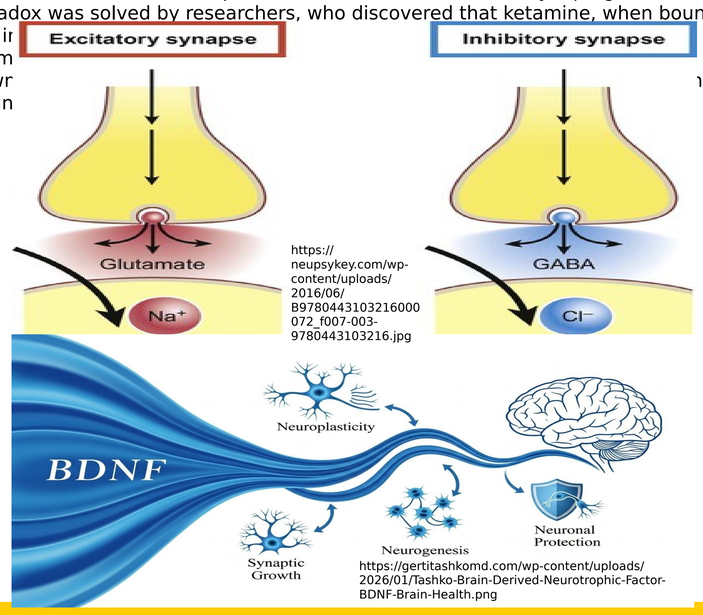
Psychopharmacological research on the use of ketamine to treat PTSD dates to the 70s, following the Vietnam War, where it was used as a battlefield anesthetic. In the early 2000s, pioneering clinicians began to explore the efficacy of the synthetic molecule in the treatment of severe depression, as selective serotonin reuptake inhibitors (SSRIs) provide symptom relief for only approximately 40% of those to whom they are prescribed, allowing ketamine to fill a much-needed gap. Typically administered intravenously in a clinical setting at a dose of 0.5–1 mg/kg of body weight in patients diagnosed with treatment-resistant depression, treatment-resistant bipolar depression, and treatment-resistant PTSD, the therapy lasts one to two hours. The dissociative anesthetic provides immediate relief of depression in most patients, and, when paired with a regimen of twice-a-week sessions for three weeks, symptom mitigation can last weeks to months.

Ketamine's mechanisms of action (Regarding Neuroplastic Benefit)

Ketamine's mechanisms of action are multiple and more complex than those of other substances that fall under the psychedelic umbrella. For this research proposal, two mechanisms have been selected as being beneficial for learning and memory during the experiment via their ability to increase neuroplasticity in the nervous system, namely *N*-methyl-D-aspartate (NMDA) receptor blocking and upregulation of brain-derived neurotrophic factor (BDNF), both leading to synaptogenesis.

NMDA receptor agonism followed by increases in BDNF

Within the nervous system are excitatory (glutamatergic) and inhibitory Gamma-Aminobutyric Acid (GABAergic) neurons that keep each other in balance. NMDA receptors, found on both, are crucial for neuroplasticity. Gibula-Tarlowski (2025) explains in her article *Ketamine—From an Anesthetic to a Psychiatric Drug* that "NMDA receptors play a key role in synaptic transmission, plasticity, and learning and memory processes" (*Molecules*). Once past the blood-brain barrier (BBB), ketamine blocks these receptors and still induces a state of synaptogenesis. This paradox was solved by researchers, who discovered that ketamine, when bound to the ir … mem … dowr … brain … for



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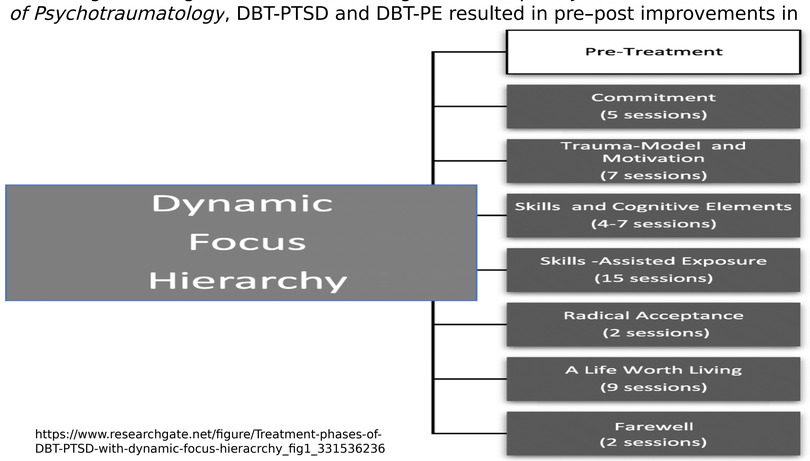
DBT-PTSD Therapy

Dialectical Behavioral Therapy–Post Traumatic Stress Disorder (DBT-PTSD) is an evidence-based modality designed for sufferers of complex trauma, combining elements of prolonged exposure therapy (PE), DBT, and compassion-focused psychotherapy.
DBT-PTSD was created to treat PTSD, C-PTSD, and BPD traits.
The duration of DBT-PTSD, when provided in an inpatient setting, is 45 days.
According to Prillinger et al. (2024), writing in the *European Journal of Psychotraumatology*, DBT-PTSD and DBT-PE resulted in pre–post improvements in


Dynamic Focus Hierarchy
Pre-Treatment
Commitment (5 sessions)
Trauma-Model and Motivation (7 sessions)
Skills and Cognitive Elements (4–7 sessions)
Skills -Assisted Exposure (15 sessions)
Radical Acceptance (2 sessions)
A Life Worth Living (9 sessions)
Farewell (2 sessions)

https://www.researchgate.net/figure/Treatment-phases-of-DBT-PTSD-with-dynamic-focus-hieracrchy_fig1_331536236

Proposed Single-blind Experiment

Hypothesis
DBT-PTSD → effective but limited for BPD remission
Ketamine → increases neuroplasticity via NMDA blockade → glutamate surge → BDNF → synaptogenesis
Hypothesis: combining them could accelerate learning + recovery
Participants receiving ketamine-assisted DBT-PTSD will show greater reductions in BPD and PTSD symptoms compared to participants receiving an active placebo and DBT-PTSD.

Recruitment
Due to typically high attrition rates, this experiment should recruit 100 randomized participants, aged 18 to 60, per group via clinical referral from psychiatric hospitals, trauma clinics, DBT programs, and outpatient providers.

Participant compensation
Due to typically high attrition rates in this population, participants will be paid $50 per day, totaling $2,250 upon completion.

Screening
Participants will complete an online or phone questionnaire. Participants must have a diagnosis of BPD with at least one Adverse Childhood Experience (ACE).

Exclusions

- Active psychosis
- Severe substance dependence
- Medical contraindications to ketamine or midazolam
- Pregnancy

Demand Characteristics
To avoid demand characteristics, control group participants will be given an active placebo (midazolam). Midazolam, often used as a placebo in ketamine studies, is an intravenous benzodiazepine commonly used for anesthesia.

Experimental group
45-day inpatient, intensive psychotherapy (DBT-PTSD) + medical intervention (low-dose ketamine) 0.5 mg/kg IV twice a week for the first three weeks.

Control group
45-day inpatient, intensive psychotherapy (DBT-PTSD) + medical intervention (midazolam) 0.3 mg/kg IV twice a week for the first three weeks.

Measures
Baseline (pretreatment): Structured Clinical Interview for DSM-5 (SCID-5)
Post-treatment and follow-ups at 3 months, 1 year, 2 years: Borderline Symptom List (BSL-23)

Ethics
This study will be conducted in accordance with the APA Ethics Code and must receive approval from an Institutional Review Board (IRB).
Cozby and Bates (2020) explain in *Methods in Behavioral Research* (14th ed.) the five principles of the APA Ethics Code:
A. Beneficence and nonmaleficence
B. Fidelity and responsibility
C. Integrity
D. Justice
E. Respect for people's rights and dignity

Informed Consent: All participants will provide written informed consent before enrollment. They will be informed of the study's purpose, procedures, potential risks, benefits, their right to withdraw at any time, and confidentiality.

Safety Monitoring: Participants receiving ketamine or midazolam will have vital signs monitored before, during, and after each infusion by trained medical staff.

Conclusion

- Ketamine-assisted DBT-PTSD may accelerate recovery in individuals with BPD and PTSD.
- Mechanism: NMDA blockade → glutamate surge → BDNF → synaptogenesis → enhanced neuroplasticity.
- Participants receiving ketamine with DBT-PTSD are expected to show greater symptom reduction compared to DBT-PTSD with placebo.
- This combined approach could shorten recovery time for this treatment-resistant population and provide a novel, evidence-based intervention for borderline personality disorder.

References

Prillinger, K., Gorelis, A., Macura, S., Hajek Gross, C., Lozar, A., Fanninger, S., Mayer, A., Oppenauer, C., Plener, P. L., & Kothgassner, O. D. (2024). A systematic review and meta-analysis on the efficacy of dialectical behavior therapy variants for the treatment of post-traumatic stress disorder. European Journal of Psychotraumatology, 15(1).
Gibuła-Tarłowska, E., Wiszniewska, A., Turyk, M., Szymczyk, P., Kotlińska, J. H., & Kędzierska, E. (2025, June 30). Ketamine-from an anesthetic to a psychiatric drug: Mechanisms of action, clinical applications and potential risks. MDPI.
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